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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,962	08/31/2000	YING CHIH CHANG	03848-00050	4091

7590 03/16/2005

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/652,962	CHANG ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4, 7 and 8 are pending and examined.

Status of the Claims

2. The amendments to the claims, filed 11/24/2004, have been entered in view of applicant's arguments and amendments to the claims and are examined.

3. The rejection of claims 1-4, 7 and 8 under 35 USC 112, second paragraph, are withdrawn in view of applicant's arguments and amendments to the claims, filed 5/28/04 and 11/24/04.

4. The rejection of claims 1-4 and 7 under 35 USC 102 or, in the alternative, under 35 USC 103, is withdrawn in view of applicant's amendments to the claims and arguments, filed 5/28/04 and 11/24/04.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-4, and 7 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hawker et al., US 6,413,587.

The claims are drawn to methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array, the method comprising: (a) providing a substrate for solid-phase synthesis of macromolecules to which one or more free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate; (b) contacting the covalently attached substrate with monomers under conditions that promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush; and (c) covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

Hawker et al., US 6,413,587, throughout the patent and at the abstract, teach methods for providing a patterned surface wherein predetermined regions of the surface are masked with a self-assembled monolayer (SAM) covalently bound to a brush polymer that are useful in biosensors and high density assay plates. Hawker et al., at col. 10, line 10-col. 11, line 5, teach methods of providing surface-bound brush polymers by derivatizing exposed functional groups of a self assembled monolayer (SAM) with a living free radical polymerization initiator followed by living free radical

polymerization of substituted or unsubstituted vinyl monomers. Hawker et al. at col. 12, lines 19-63, teach fabricating biosensors by providing a patterned SAM functionalized with an overlying polymeric brush, wherein the "free" termini of the brush polymers have exposed functionalities including, for example, antigen, antibody, or any variety of specific or non-specific substrates for binding and thereby detecting a particular binding molecule. It would have been obvious to covalently attach a plurality of macromolecules to a plurality of reactive groups on a polymeric brush because Hawker et al., at col. 9, lines 24 teaches that fabrication of biosensors and high-density assay plates, wherein an antigen, antibody, hapten, etc., is covalently bound to a self-assembled monolayer was known in the art, as evidenced by Kumar et al., (U.S. Pat. No. 5,512,131, see col. 11, lines 31-63). It is noted that Hawker et al., in col. 12, line 24, refer to Kumar et al. for this purpose.

New Claim Rejections - 35 USC § 103

6. Claims 1-4, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hawker et al., US 6,413,587; and Mrksich et al., (TibTech June 1995, Vol. 13, pp. 228-235).

The claims are drawn to methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array, the method comprising: (a) providing a substrate for solid-phase synthesis of macromolecules to which one or more free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate; (b) contacting the covalently attached substrate with monomers under conditions that

promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush; and (c) covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

Hawker et al., US 6,413,587, throughout the patent and at the abstract, teach methods for providing a patterned surface wherein predetermined regions of the surface are masked with a self-assembled monolayer (SAM) covalently bound to a brush polymer that are useful in biosensors and high density assay plates. Hawker et al., at col. 10, line 10-col. 11, line 5, teach methods of providing surface-bound brush polymers by derivatizing exposed functional groups of a self assembled monolayer (SAM) with a living free radical polymerization initiator followed by living free radical polymerization of substituted or unsubstituted vinyl monomers. Hawker et al. at col. 12, lines 19-63, teach fabricating biosensors by providing a patterned SAM functionalized with an overlying polymeric brush, wherein the "free" termini of the brush polymers have exposed functionalities including, for example, antigen, antibody, or any variety of specific or non-specific substrates for binding and thereby detecting a particular binding molecule.

Hawker et al. do not disclose *covalently* attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

Mrksich et al., throughout the publication, and especially at p. 229, para 2, and Table 2, teach attaching peptides and proteins to the organic surfaces of a SAM, after the SMA is formed, through functional groups on the SAM (including $-NH_2$) reacting with a functional group on the protein ($-CO_2H$). Mrksich et al. at p. 230, para 6-p. 230,

para 1, teach photolithography for creating patterned monolayers to form a SAM. Mrksich et al. at p. 231, para 3, teach immobilizing proteins onto a surface containing patterned regions of a reactive functional group and the production of arrays of hundreds of different peptides and antibodies by combining solid-phase organic synthesis with photolithographic techniques.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have used methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array by covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

One of ordinary skill in the art would have been motivated to create an array of macromolecules, including peptides or antibodies, covalently attached to a polymeric brush on a substrate in order to create patterned biosensors for detecting target molecules that bind the antibodies or peptides, as taught by Hawker and Mrksich. One of ordinary skill in the art would had a reasonable expectation of success in covalently attaching a plurality of the peptides or antibodies to the polymeric brush, because Mrksich et al. teach functional groups on a SAM, including amino groups, for reacting with proteins, and because Mrksich et al. teach the attachment of proteins to a SAM (considered here to include a polymeric brush) using photolithographic methods.

7. Claims 1-4, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., (Anal. Chem. 1997, 69, 4577-4580; on PTO-1449); Hawker et al., US 6,413,587; and Mrksich et al., (TibTech June 1995, Vol. 13, pp. 228-235).

The claims are drawn to methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array, the method comprising: (a) providing a substrate for solid-phase synthesis of macromolecules to which one or more free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate; (b) contacting the covalently attached substrate with monomers under conditions that promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush; and (c) covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

Huang et al. disclose a method of surface-initiated radical polymerization on silica that reads on the claimed method (see Abstract and Scheme 2). Specifically, the reference discloses "preparing polymeric thin films" where "living radicals are used to greatly improve the control of the reaction" (page 4577, 2nd column, bottom). The thin film of the reference reads on the claimed "polymeric brush". As shown in Scheme 2, benzyl chloride free radical initiators are covalently attached to a silica surface (also see description of reaction in Scheme 1). This reads directly on the claimed "radical generation site distal to the substrate" and also on the limitations of instant claim 3. Vinyl-containing monomers are reacted with the benzyl chloride free radical initiators on the surface via a living radical polymerization (see page 4578, 1st column and Schemes

1 & 2); this reads directly on the limitations of instant claims 2 and 4. Also as shown in Scheme 2, the polymer thin film product formed by the method of Huang et al contains amino groups, reading on the instant claim 7.

Huang et al. do not disclose covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

Hawker et al., US 6,413,587, throughout the patent and at the abstract, teach methods for providing a patterned surface wherein predetermined regions of the surface are masked with a self-assembled monolayer (SAM) covalently bound to a brush polymer that are useful in biosensors and high density assay plates. Hawker et al., at col. 10, line 10-col. 11, line 5, teach methods of providing surface-bound brush polymers by derivatizing exposed functional groups of a self assembled monolayer (SAM) with a living free radical polymerization initiator followed by living free radical polymerization of substituted or unsubstituted vinyl monomers. Hawker et al. at col. 12, lines 19-63, teach fabricating biosensors by providing a patterned SAM functionalized with an overlying polymeric brush, wherein the "free" termini of the brush polymers have exposed functionalities including, for example, antigen, antibody, or any variety of specific or non-specific substrates for binding and thereby detecting a particular binding molecule.

Mrksich et al., throughout the publication, and especially at p. 229, para 2, and Table 2, teach attaching peptides and proteins to the organic surfaces of a SAM, after the SMA is formed, through functional groups on the SAM (including $-NH_2$) reacting with a functional group on the protein ($-CO_2H$). Mrksich et al. at p. 230, para 6-p. 230,

para 1, teach photolithography for creating patterned monolayers to form a SAM. Mrksich et al. at p. 231, para 3, teach immobilizing proteins onto a surface containing patterned regions of a reactive functional group and the production of arrays of hundreds of different peptides and antibodies by combining solid-phase organic synthesis with photolithographic techniques.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have used methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array by covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush.

One of ordinary skill in the art would have been motivated to create an array of macromolecules, including peptides or antibodies, covalently attached to a polymeric brush on a substrate in order to create patterned biosensors for detecting target molecules that bind the antibodies or peptides, as taught by Hawker and Mrksich. One of ordinary skill in the art would had a reasonable expectation of success in covalently attaching a plurality of the peptides or antibodies to the polymeric brush, because Huang et al. teach a polymeric brush with amino groups, which Mrksich et al. teach as a functional group for reacting with proteins, and because Mrksich et al. teach the attachment of proteins to a SAM (considered here to include a polymeric brush) using photolithographic methods.

8. Claims 1-4, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hawker et al., US 6,413,587; and Mrksich et al., (TibTech June 1995, Vol. 13, pp. 228-235) as applied to claims 1-7 and 7 above, and further in view of Mardare et al., US 5,312,871.

The claims are drawn to methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array, the method comprising: (a) providing a substrate for solid-phase synthesis of macromolecules to which one or more free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate; (b) contacting the covalently attached substrate with monomers under conditions that promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush; and (c) covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush; and wherein the monomers comprise vinyl acetate.

None of Hawker et al. or Mrksich et al. teach methods comprising polymeric brush substrates wherein the monomers comprise vinyl acetate.

Mardare et al., at col. 1, lines 11-27 teach free radical polymerization processes, and col. 2, lines 1-62, teach living polymerization where the preferred monomers are vinyl acetate (col. 2, lines 12 and 42).

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art to have made a polymeric brush substrate wherein the monomers comprise vinyl acetate.

One of ordinary skill in the art would have been motivated to use vinyl acetate monomers because Mardare et al. teach that polymers comprising vinyl acetate are especially useful in the preparation of films and Huang teaches "preparing polymeric thin films" that read on polymeric brush substrates. One of ordinary skill in the art would have had a reasonable expectation of success in using vinyl acetate monomers because Hawker et al. teach the use of substituted vinyl monomers in making their polymeric brushes by living free radical polymerization.

9. Claims 1-4, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., (Anal. Chem. 1997, 69, 4577-4580; on PTO-1449); Hawker et al., US 6,413,587; and Mrksich et al., (TibTech June 1995, Vol. 13, pp. 228-235) as applied to claims 1-7 and 7 above, and further in view of Mardare et al., US 5,312,871.

The claims are drawn to methods of preparing a polymeric brush substrate having a plurality of macromolecules thereon for use in a macromolecular array, the method comprising: (a) providing a substrate for solid-phase synthesis of macromolecules to which one or more free radical initiators are covalently attached, wherein each free radical initiator has a radical generation site distal to the substrate; (b) contacting the covalently attached substrate with monomers under conditions that promote free radical polymerization from the radical generation sites of the initiators to form a polymeric brush; and (c) covalently attaching a plurality of macromolecules to a plurality of reactive groups on the polymeric brush; and wherein the monomers comprise vinyl acetate.

None of Huang et al., Hawker et al., or Mrksich et al. teach methods comprising polymeric brush substrates wherein the monomers comprise vinyl acetate.

Mardare et al., at col. 1, lines 11-27 teach free radical polymerization processes, and col. 2, lines 1-62, teach living polymerization where the preferred monomers are vinyl acetate (col. 2, lines 12 and 42).

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the art to have made a polymeric brush substrate wherein the monomers comprise vinyl acetate.

One of ordinary skill in the art would have been motivated to use vinyl acetate monomers because Mardare et al. teach that polymers comprising vinyl acetate are especially useful in the preparation of films and Huang teaches "preparing polymeric thin films" that read on polymeric brush substrates. One of ordinary skill in the art would have had a reasonable expectation of success in using vinyl acetate monomers because Hawker et al. teach the use of substituted vinyl monomers in making their polymeric brushes by living free radical polymerization.

Conclusion

10. Claims 1-4, 7 and 8 are rejected.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

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